Revolution Medicines to Present Preclinical Data on Innovative Mutant-Targeted Catalytic RAS(ON) Inhibitor at the 2026 AACR Annual Meeting

April 21, 2026

Data highlight RM-055's ability to overcome resistance and provide deep, durable antitumor activity across preclinical models of pancreatic ductal adenocarcinoma, non-small cell lung cancer and colorectal cancer

REDWOOD CITY, Calif., April 21, 2026 (GLOBE NEWSWIRE) -- Revolution Medicines, Inc. (Nasdaq: RVMD), a late-stage clinical oncology company developing targeted therapies for patients with RAS-addicted cancers, today announced preclinical data highlighting an innovative new class of mutant-targeted catalytic RAS(ON) inhibitors. These catalytic inhibitors are designed to promote the conversion of mutant RAS in its active RAS(ON) state back to the inactive RAS(OFF) state thereby mimicking the physiological regulation of wild type RAS. This mechanism represents a differentiated approach to inhibition of oncogenic RAS signaling with the goal of addressing tumor resistance mechanisms and extending the durability of current RAS-targeted therapies.

Results will be presented during a mini symposium at the American Association for Cancer Research (AACR) Annual Meeting on April 21, 2026 (Abstract #6782).

“Additional strategies are needed to counter emergent resistance to RAS inhibitors and further extend clinical benefit for patients with RAS mutant cancers,” said Jan Smith, Ph.D., chief scientific officer, Revolution Medicines. “Using our cyclophilin A tri-complex platform, we have discovered a new class of mutant-targeted RAS(ON) catalytic inhibitors designed to stimulate the GTPase activity of mutant RAS variants, a long-sought goal of the RAS research community. In preclinical models, RM-055, an oral compound with this mechanism as the primary driver of RAS pathway inhibition, drove deep and durable tumor regressions across multiple tumor types and overcame resistance to prior RAS inhibition.”

At well-tolerated doses, RM-055 demonstrated robust and durable antitumor activity across KRAS G12 mutant xenograft models of pancreatic ductal adenocarcinoma, non-small cell lung cancer, and colorectal cancer. Notably, tumors that had escaped prior RAS inhibitor treatment were sensitive to RM-055, which drove deep and durable regressions warranting further investigation of its potential to counter emergent drug resistance and extend clinical benefit.

Mutant RAS variants causing cancer are relatively insensitive to the natural GTPase-activating proteins (GAPs) that induce physiological inactivation of wild type RAS by stimulating hydrolysis of RAS-GTP to RAS-GDP. Similar to the natural GAPs, RM-055 accelerates the hydrolysis of mutant RAS-GTP to RAS-GDP, converting oncogenic RAS from its active RAS(ON) state to an inactive RAS(OFF) state. A single cyclophilin A:RM-055 binary complex can inactivate multiple mutant RAS proteins.

In preclinical studies, RM-055 significantly reduced RAS-GTP levels in cells, leading to inhibition of downstream RAS signaling and tumor cell proliferation. *In vivo* RM-055 preferentially suppressed RAS pathway activation in KRAS G12 mutant tumors over normal tissues. This mutant-targeted activity, with a reduced impact on wild-type RAS in normal tissues, suggests the potential for an enhanced therapeutic window and increased flexibility for combination approaches. Moreover, this approach may enable durable pathway suppression even in tumors with increased RAS signaling, a common mechanism of clinical acquired resistance to RAS inhibition.

This novel class of catalytic inhibitors complements Revolution Medicines’ broad portfolio of RAS(ON) multi- and mutant-selective inhibitors that act primarily through steric inhibition of RAS(ON) and further highlights the potential of the cyclophilin A tri-complex platform to enable chemical mechanisms that have not been achieved previously with conventional small molecule strategies.

About Revolution Medicines, Inc.
Revolution Medicines is a late-stage clinical oncology company developing novel targeted therapies for patients with RAS-addicted cancers. The company’s R&D pipeline comprises RAS(ON) inhibitors designed to suppress diverse oncogenic variants of RAS proteins. The company’s RAS(ON) inhibitors daraxonrasib (RMC-6236), a RAS(ON) multi-selective inhibitor; elironrasib (RMC-6291), a RAS(ON) G12C-selective inhibitor; zoldonrasib (RMC-9805), a RAS(ON) G12D-selective inhibitor; and RMC-5127, a RAS(ON) G12V-selective inhibitor, are currently in clinical development. Additional development opportunities in the company’s pipeline focus on RAS(ON) mutant-selective inhibitors, including RMC-0708 (Q61H) and RMC-8839 (G13C). For more information, please visit www.revmed.com and follow us on LinkedIn.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995. Any statements in this press release that are not historical facts may be considered “forward-looking statements,” including without limitation statements regarding the company’s development strategy and its ability to build or advance its portfolio and R&D pipeline; progression of clinical studies and findings from these studies, including the tolerability, safety, and potential efficacy of the company’s candidates being studied; findings from the company’s preclinical studies and the ability of these studies to predict clinical outcomes; and then therapeutic impact of a molecule’s mechanism of action, including the therapeutic potential of the company’s new class of mutant-targeted catalytic RAS(ON) inhibitors.

Forward-looking statements are typically, but not always, identified by the use of words such as “aims,” “anticipate,” "believe," "estimate," "expect," "plan," “potential,” “project,” “up to,” "will" and other similar terminology indicating future results. Such forward-looking statements are subject to substantial risks and uncertainties that could cause the company’s development programs, future results, performance, or achievements to differ materially from those anticipated in the forward-looking statements. Such risks and uncertainties include without limitation risks and uncertainties inherent in the drug development process, including the company’s programs’ development stages, the process of designing and conducting preclinical and clinical trials, the regulatory approval processes, the timing of regulatory filings, the challenges associated with manufacturing drug products, the company’s ability to successfully establish, protect and defend its intellectual property, other matters that could affect the sufficiency of the company’s capital resources to fund operations, reliance on third parties for manufacturing and development efforts, changes in the competitive landscape, and the effects on the company’s business of the global events, such as international conflicts or global pandemics. For a further description of the risks and uncertainties that could cause actual results to differ from those anticipated in these forward-looking statements, as well as risks relating to the business of Revolution Medicines in general, see Revolution Medicines’ Annual Report on Form 10-K filed with the Securities and Exchange Commission (the “SEC”) on February 25, 2026, and its future periodic reports to be filed with the SEC. Except as required by law, Revolution Medicines undertakes no obligation to update any forward-looking statements to reflect new information, events, or circumstances, or to

reflect the occurrence of unanticipated events.

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